

### Remarks/Arguments

Claims 1-18 and 23-36 are pending in this Application. In the Office Action mailed May 19, 2003, the Examiner:

rejected claims 1-8, 13-18, and 23-36 under 35 U.S.C. § 102(b) as being anticipated by US Patent 5,407,609 to Tice et al.;

rejected claims 8-11 under U.S.C. § 103(a) as being unpatentable over Tice et al., in view of US Patent 5,622,657 to Takada et al.; and

rejected claim 101 and 103 under U.S.C. § 103(a) as being unpatentable over Tice et al., in view of Baker et al.

Applicants respectfully address the basis for each of the Examiner's rejections below.

#### ***Claim Rejections – 35 U.S.C. §102 (b) – Claims 1-8, 13-18, 23-26***

The Examiner rejected Claims 1-8, 13-18, and 23-36 under 35 U.S.C. § 102(b) as being anticipated by U.S. Patent 5,407,609 to Tice et al. The Examiner stated:

Tice et al. teach a method of encapsulating an agent. Tice et al. teach that a suitable wall forming material, such as a polymer, is first dissolved or otherwise dispersed in a solvent (c 3, l 50-52). The liquid or solid agent to be encapsulated is then dispersed or dissolved in the solvent containing the dissolved wall forming material (c 4, l 30-32). This mixture is then added to a continuous process medium to form microdroplets (c 5, l 50-52). The process medium is then mechanically agitated with devices such as homogenizers, propellers or the like (c 6, l 9-12). Once the emulsion is formed, the process medium is transferred to an extraction medium so that the solvent can be removed from the microdroplets (c 6, l 23-27). Lastly, the microcapsules or microspheres are collected by centrifugation, filtration or the like (c 6, l 42-46).

Applicants respectfully submit that Tice et al. does not anticipate Applicants' Claims 1-8, 13-18 and 23-36, because Tice et al. does not identically disclose Applicants' claimed invention. The Examiner is correct that Tice et al. discloses "a method of microencapsulating an agent;" however, the method disclosed by Tice et al. is substantially different than that claimed by the

Applicants. Tice et al. teaches that microdroplets are formed “after the agent is added to the wall material/excipient solvent, [and] the agent/(wall material-excipient)/solvent mixture dispersion is added to a continuous process medium.” (Col. 5, ll. 50-54) With the present invention, microspheres are produced by “extracting the organic solvent from the emulsion.” (Claim 1, ll. 9)

As such, Tice et al. does not teach each and every limitation of Applicants' instant claims and each and every limitation thereof are not identical or anticipated by Tice et al. Applicants respectfully request the rejection to Claim 1 and those depending from Claim 1, namely Claims 2-8, 13-18, and 25-36, as well as Claims 23 and 24 be withdrawn under 35 U.S.C. § 102(e).

***Claim Rejections – 35 U.S.C. §103(a) – Claims 8-11***

The Examiner rejected Claims 8-11 under U.S.C. § 103(a) as being unpatentable over Tice et al. in view of U.S. Patent 5,622,657 to Takada et al.

While the Examiner finds teachings within Tice et al., for encapsulating an agent, Applicants find no disclosure or suggestion within Tice et al., for *a method further comprising stabilizing the bioactive substance; wherein the bioactive substance is stabilized with a carrier protein; wherein the carrier protein comprises albumin; and wherein the bioactive substance is stabilized by maximizing the concentration of the substance in the solution, by adding a metal to the solution, by adding gelatin to the solution, or by adding a small osmolyte to the solution* as claims 8-11 requires.

The Examiner goes on to state:

Tice et al do not teach that the bioactive substance is stabilized with a carrier protein, such as albumin.

Applicants agree with the Examiner, because the method for encapsulating an agent as disclosed by Tice et al. is substantially different than that claimed by Applicants. Applicants also respectfully disagree with the Examiner's interpretation of Tice et al. in view of Takada et al. Neither Tice et al. nor Takada et al. teach or suggest all the claim limitations of the instant invention. As described above, the Tice et al. reference is “as a whole” an entirely different method for encapsulation. In order for one or more references to be obvious, there must also be

some suggestion or motivation to modify the reference and a reasonable expectation of success. Applicants can find no suggestion or motivation within Tice et al.'s method of microencapsulating an agent to combine it with the teachings of Takada et al.'s methods for coating microparticles by "spraying a solution of a polymer containing a drug and an aqueous solution of an agent for preventing aggregation" using "different nozzles and contacting them with each other in a spray dryer" (See Abstract and Col 2. ll. 38-54), nor is there any reasonable expectation that such an undertaking would be successful.

Further, Takada et al. does not teach stabilization of an agent during microencapsulation. Rather, the reference teaches albumin may be used as an "aggregation-preventing agent" that is "sprayed" as a film "to coat the surface of the microparticle" that is already prepared. (Col. 2, ll. 48-54) Accordingly, Applicants respectfully submit that the combination of Tice et al. and Takada et al., fails to render the present invention obvious. In fact, there is no motivation in Tice et al. or Takada et al. to prompt one of ordinary skill to selectively and non-inventively modify such references, nor is there any reasonable expectation that such an undertaking would be successful.

As such, Applicants submit that Claims 8-11 are patentably distinguishable over the art cited and in condition for allowance.

***Claim Rejections – 35 U.S.C. §103(a) – Claim 12***

The Examiner rejected Claim 12 under U.S.C. § 103(a) as being unpatentable over Tice et al. in view of Baker et al.

As discussed above, Applicants respectfully disagree with the Examiner's interpretation of the Tice et al. reference. For the reasons stated above, Tice et al. discloses a different method of encapsulation and, therefore, cannot, when used alone or in combination with another invention, render the present invention obvious.

Further, in order for one or more references to be obvious, there must also be some suggestion or motivation to modify the reference and a reasonable expectation of success.

Applicants can find no suggestion or motivation within Tice et al.'s method of microencapsulating an agent to combine it with the teachings of Baker et al.'s "method for universally distributing a therapeutic agent to the brain" using "intrathecal administration." (See Abstract and Col 2, ll. 5-8) nor is there any reasonable expectation that such an undertaking, if ever taken, would be successful.

The MPEP also states, "to rely on a reference under 35 U.S.C 103, it must be analogous prior art." MPEP 2141.01(a). Applicants submit that the Baker et al. reference of methods for universally distributing therapeutic agents to the brain is not in the same field as the Applicants' nor is the Baker et al. reference reasonably pertinent to the Applicants' problem with prior art methods, including "the use of a single polymer species such as PLGA alone, or a PLGA/poly (eta-caprolactine) to fabricate the microspheres" (Specification pg. 5, ll. 7-9) and "use of a tissue homogenizer to form the polymer emulsion" (Specification pg. 6, ll. 3-5), because a person of ordinary skill seeking to solve a problem of providing a solid-encapsulation/single-emulsion/solvent extraction technique is not reasonably expected or motivated to look to a method of intrathecally administering a therapeutic agent to the brain, especially in a reference that is "for the amelioration of stroke and/or Traumatic Brain Injury." (Abstract). Accordingly, Applicants respectfully submit that Claim 12 is patentably distinguishable over the art cited, and thus allowable.

### Conclusion

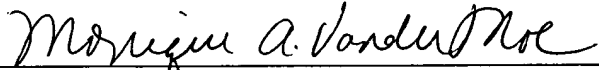
In light of the amendments, remarks and arguments presented above, Applicants respectfully submit that the claims in the Application are in condition for allowance. Favorable consideration and allowance of the pending claims is therefore respectfully requested.

Enclosed herewith is our firm's check in the amount of \$55.00 to cover the filing fee for the one (1) month extension of time. It is believed that no additional fee is due. If this is incorrect, the Commissioner is hereby authorized to charge any fees, other than an issue fee that may be required by this paper to our Deposit Account No.07-0153..

If the Examiner has any questions or comments, or if further clarification is required, it is requested that the Examiner contact the undersigned at the telephone number listed below.

Dated: September 19, 2003.

Respectfully submitted,  
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